

AMENDMENTS TO THE SPECIFICATION:

Please delete the paragraphs beginning at page 6, line 2, in their entirety and insert the following new paragraphs in lieu thereof:

Figures 1A-1D: Generation and expression of the group M consensus env gene (CON6). The complete amino acid sequence of CON6 gp160 is shown. (Fig. 1A) (SEQ ID NO: 1) The five regions from the wild-type CRF08\_BC (98CN006) env gene are indicated by underlined letters. Variable regions are indicated by brackets above the sequences. Potential N-linked glycosylation sites are highlighted with bold-faced letters. (Fig. 1B) Constructs of CON6 gp120 and gp140CF. CON6 gp120 and gp140CF plasmids were engineered by introducing a stop codon after the gp120 cleavage site or before the transmembrane domain, respectively. The gp120/gp41 cleavage site and fusion domain of gp41 were deleted in the gp140CF protein. (Fig. 1C) Expression of CON6 gp120 and gp140CF. CON6 gp120 and gp140CF were purified from the cell culture supernatants of rVV-infected 293T cells with *galanthus Nivalis* agarose lectin columns. Both gp120 and gp140CF were separated on a 10% SDS-polyarylamide gel and stained with Commassie blue. (Fig. 1D.) (SEQ ID NO: 2) CON6 env gene optimized based on codon usage for highly expressed human genes.

Figures 2A-2E. Binding of CON6 gp120 gp140 CF to soluble CD4 (sCD4) and anti-Env mAbs. (Figs. 2A-2B) Each of the indicated mabs and sCD4 was covalently immobilized to a CM5 sensor chip (BIAcore) and CON6 gp120 (Fig. 2A) or gp140CF (Fig. 2B) (100 µg/ml and 300 µg/ml, respectively) were injected over

each surface. Both gp120 and gp140CF proteins reacted with each anti-gp120 mabs tested except for 17b mab, which showed negligible binding to both CON6 gp120 and gp140CF. To determine induction of 17b mab binding to CON6 gp120 and gp140CF, CON6 gp120 (Fig. 2C) or gp140CF (Fig. 2D) proteins were captured (400-580 RU) on individual flow cells immobilized with sCD4 or mabs A32 or T8. Following stabilization of each of the surface, mAb 17b was injected and flowed over each of the immobilized flow cells. Overlay of curves show that the binding of mab 17b to CON6 Env proteins was markedly enhanced on both sCD4 and mab A32 surfaces but not on the T8 surface (Figs. 2C-2D). To determine binding of CON6 gp120 and gp140CF to human mabs in ELISA, stock solutions of 20 µg/ml of mabs 447, F39F, A32, IgG1b12 and 2F5 on CON6 gp120 and gp140CF were tittered (Fig. 2E). Mabs 447 (V3), F39F (V3) A32 (gp120) and IgG1b12 (CD4 binding site) each bound to both CON6 gp120 and 140 well, while 2F5 (anti-gp41 ELDKWS) (SEQ ID NO: 321) only bound gp140CF. The concentration at endpoint titer on gp120 for mab 447 and F39F binding was <0.003 µg/ml and 0.006 µg/ml, respectively; for mab A32 was <0.125 µg/ml; for IgG1b12 was <0.002 µg/ml; and for 2F5 was 0.016 µg/ml.

Please delete the paragraph beginning at page 9, line 21, in its entirety and insert the following new paragraph in lieu thereof:

Figures 6A-6E. Construction of codon usage optimized subtype C ancestral and consensus envelope genes (Figs. 6A and 6B, respectively) (SEQ ID NOS 3-4). Ancestral and consensus amino acid sequences (Figs. 6C and 6D, respectively) (SEQ ID NOS

5-6) were transcribed to mirror the codon usage of highly expressed human genes. Paired oligonucleotides (80-mers) overlapping by 20 bp were designed to contain 5' invariant sequences including the restriction enzyme sites EcoRI, BbsI, Bam HI and BsmBI. BbsI and BsmBI are Type II restriction enzymes that cleave outside of their recognition sequences. Paired oligomers were linked individually using PCR and primers complimentary to the 18 bp invariant sequences in a stepwise fashion, yielding 140bp PCR products. These were subcloned into pGEM-T and sequenced to confirm the absence of inadvertant mutations/deletions. Four individual pGEM-T subclones containing the proper inserts were digested and ligated together into pcDNA3.1. Multi-fragment ligations occurred repeatedly amongst groups of fragments in a stepwise manner from the 5' to the 3' end of the gene until the entire gene was reconstructed in pcDNA3.1. (See schematic in Fig. 6E.)

Please delete the paragraph beginning at page 11, line 6, in its entirety and insert the following new paragraph in lieu thereof:

Figure 8. Sequence alignment of subtype C ancestral and consensus env genes. Alignment of the subtype C ancestral (bottom line) (SEQ ID NO: 8) and consensus (top line) (SEQ ID NO: 7) env sequences showing a 95.5% sequence homology; amino acid sequence differences are indicated. One noted difference is the addition of a glycosylation site in the C ancestral env gene at the base of the V1 loop. A plus sign indicates a within-class difference of amino acid at the indicated position; a bar indicates a change in the class of amino acid. Potential N-

glycosylation sites are marked in blue. The position of truncation for the gp140 gene is also shown.

Please delete the paragraphs beginning at page 14, line 12, in their entirety and insert the following new paragraphs in lieu thereof:

Figures 13A-13F. Protein expression of consensus subtype C Gag (Fig. 13A) and Nef (Fig. 13B) following transfection into 293T cells. Consensus subtype C Gag and Nef amino acid sequences are set forth in Figs. 13C and 13D, respectively, (SEQ ID NOS 9-10) and encoding sequences are set forth in Figs. 13E and 13F, respectively (SEQ ID NOS 11-12).

Figures 14A-14C. Figs. 14A and 14B show the Con-S Env amino acid sequence and encoding sequence, respectively (SEQ ID NOS 13-14). Fig. 14C shows expression of Group M consensus Con-S Env proteins using an *in vitro* transcription and translation system.

Please delete the paragraphs beginning at page 15, line 7, in their entirety and insert the following new paragraphs in lieu thereof:

Figures 18A-18D. Figs. 18A and 18B show subtype A consensus Env amino acid sequence and nucleic acid sequence encoding same, respectively (SEQ ID NOS 15-16). Figs. 18C and 18D show expression of A.con env gene in mammalian cells (Fig. 18C - cell lysate, Fig. 18D - supernatant).

Figures 19A-19H. M.con.gag (Fig. 19A) (SEQ ID NO: 17), M.con.pol (Fig. 19B) (SEQ ID NO: 18), M.con.nef (Fig. 19C) (SEQ ID NO: 19) and C.con.pol (Fig. 19D) (SEQ ID NO: 20) nucleic acid sequences and corresponding encoded amino acid sequences (Figs. 19E-19H, respectively) (SEQ ID NOS 21-24).

Figures 20A-20D. Subtype B consensus gag (Fig. 20A) (SEQ ID NO: 25) and env (Fig. 20B) (SEQ ID NO: 26) genes. Corresponding amino acid sequences are shown in Figs. 20C and 20D (SEQ ID NOS 28-29).

Please delete the paragraph beginning at page 19, line 11, in its entirety and insert the following new paragraph in lieu thereof:

Figures 26A and 26B. Fig. 26A. 2000 Con-S 140CFI.ENV (SEQ ID NO: 30). Fig. 26B. Codon-optimized Year 2000 Con-S 140CFI.seq (SEQ ID NO: 31).

Please delete the paragraph beginning at page 19, line 25, in its entirety and insert the following new paragraph in lieu thereof:

Figures 28A-28C. Fig. 28A. Con-B 2003 Env. pep (841 a.a.) (SEQ ID NO: 32). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 28B. Con-B-

140CF.pep (632 a.a.) (SEQ ID NO: 33). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 28C. Codon-optimized Con-B 140CF.seq (1927 nt.) (SEQ ID NO: 34).

Please delete the paragraphs beginning at page 20, line 8, in their entirety and insert the following new paragraphs in lieu thereof:

Figures 29A-29C. Fig. 29A. CON\_OF\_CONS-2003 (829 a.a.) (SEQ ID NO: 35). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 29B. Cons-2003 140CF.pep (620 a.a.) (SEQ ID NO: 36). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 29C. CODON-OPTIMIZED Cons-2003 140CF.seq (1891 nt.) (SEQ ID NO: 37).

Figures 30A-30C. Fig. 30A. CONSENSUS\_A1-2003 (845 a.a.) (SEQ ID NO: 38). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 30B. Con-A1-2003 140CF.pep (629 a.a.) (SEQ ID NO: 39). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 30C. CODON-OPTIMIZED Con-A1-2003.seq (SEQ ID NO: 40).

Figures 31A-31C. Fig. 31A. CONSENSUS\_C-2003 (835 a.a.) (SEQ ID NO: 41). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 31B. Con-C 2003 140CF.pep (619 a.a.) (SEQ ID NO: 42). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 31C. CODON-OPTIMIZED Con-C-2003 (140 CF (1,888 nt.) (SEQ ID NO: 43).

Figures 32A-32C. Fig. 32A. CONSENSUS\_G-2003 (842 a.a.) (SEQ ID NO: 44). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 32B. Con-G-2003 140CF.pep (626 a.a.) (SEQ ID NO: 45). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 32C. CODON-OPTIMIZED Con-G-2003.seq (SEQ ID NO: 46).

Figures 33A-33C. Fig. 33A. CONSENSUS\_01\_AE-2003 (854 a.a.) (SEQ ID NO: 47). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 33B. Con-AE01-2003 140CF.pep (638 a.a.) (SEQ ID NO: 48). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 33C. CODON-OPTIMIZED Con-AE01-2003.seq. (1945 nt.) (SEQ ID NO: 49).

Figures 34A-34C. Fig. 34A. Wild-type subtype A Env. 00KE\_MSA4076-A (Subtype A, 891 a.a.) (SEQ ID NO: 50). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 34B. 00KE\_MSA4076-A 140CF.pep (647 a.a.) (SEQ ID NO: 51). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 34C. CODON-OPTIMIZED 00KE\_MSA4076-A 140CF.seq. (1972 nt.) (SEQ ID NO: 52).

Figures 35A-35C. Fig. 35A. Wild-type subtype B. QH0515.1g gp160 (861 a.a.) (SEQ ID NO: 53). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 35B. QH0515.1g 140CF (651 a.a.) (SEQ ID NO: 54). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 35C. CODON-OPTIMIZED QH0515.1g 140CF.seq (1984 nt.) (SEQ ID NO: 55).

Figures 36A-36C. Fig. 36A. Wild-type subtype C. DU123.6 gp160 (854 a.a.) (SEQ ID NO: 56). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 36B. DU123.6 140CF (638 a.a.) (SEQ ID NO: 57). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 36C. CODON-OPTIMIZED DU123.6 140CF.seq (1945 nt.) (SEQ ID NO: 58).



Figures 37A-37C. Fig. 37A. Wild-type subtype CRF01\_AE. 97CNGX2F-AE (854 a.a.) (SEQ ID NO: 59). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 37B. 97CNGX2F-AE 140CF.pep (629 a.a.) (SEQ ID NO: 60). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 37C. CODON-OPTIMIZED 97CNGX2F-AE 140CF.seq (1921 nt.) (SEQ ID NO: 61).

Figures 38A-38C. Fig. 38A. Wild-type DRCBL-G (854 a.a.) (SEQ ID NO: 62). Amino acid sequence underlined is the fusion domain that is deleted in 140CF design and the "W" underlined is the last amino acid at the C-terminus, all amino acids after the "W" are deleted in the 140CF design. Fig. 38B. DRCBL-G 140CF.pep (630 a.a.) (SEQ ID NO: 63). Amino acids in bold identify the junction of the deleted fusion cleavage site. Fig. 38C. CODON-OPTIMIZED DRCBL-G 140CF.seq (1921 nt.) (SEQ ID NO: 64).

Figures 39A and 39B. Fig. 39A. 2003 Con-S Env (SEQ ID NO: 65). Fig. 39B. 2003 Con-S Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 72)

Figures 40A and 40B. Fig. 40A. 2003 M. Group.Anc Env (SEQ ID NO: 66). Fig. 40B. 2003 M. Group.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 67)

Figures 41A and 41B. Fig. 41A. 2003 CON\_A1 Env (SEQ ID NO: 68). Fig. 41B. 2003 CON\_A1 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 70)

Figures 42A and 42B. Fig. 42A. 2003 A1.Anc Env (SEQ ID NO: 69). Figs. 42B. 2003 A1.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 71)

Figures 43A and 43B. Fig. 43A. 2003 CON\_A2 Env (SEQ ID NO: 73). Fig. 43B. 2003 CON\_A2 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 75)

Figures 44A and 44B. Fig. 44A. 2003 CON\_B Env (SEQ ID NO: 74). Fig. 44B. 2003 CON\_B Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 76)

Figures 45A and 45B. Fig. 45A. 2003 B.anc Env (SEQ ID NO: 77). Figs. 45B. 2003 B.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 79)

Figures 46A and 46B. Fig. 46A. 2003 CON\_C Env (SEQ ID NO: 78). Fig. 46B. 2003 CON\_C Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 80)

Figures 47A and 47B. Fig. 47A. 2003 C.anc Env (SEQ ID NO: 81). Fig. 47B. 2003 C.anc Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 83)

Figures 48A and 48B. Fig. 48A. 2003 CON\_D Env (SEQ ID NO: 82). Fig. 48B. 2003 CON\_D Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 84)

Figures 49A and 49B. Fig. 49A. 2003 CON\_F1 Env (SEQ ID NO: 85). Fig. 49B. 2003 CON\_F1 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 87)

Figures 50A and 50B. Fig. 50A. 2003 CON\_F2 Env (SEQ ID NO: 86). Fig. 50B. 2003 CON\_F2 Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 88)

Figures 51A and 51B. Fig. 51A. 2003 CON\_G Env (SEQ ID NO: 89). Fig. 51B. 2003 CON\_G Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 91)

Figures 52A and 52B. Fig. 52A. 2003 CON\_H Env (SEQ ID NO: 90). Fig. 52B. 2003 CON\_H Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 92)

Figures 53A and 53B. Fig. 53A. 2003 CON\_01\_AE Env (SEQ ID NO: 93). Fig. 53B. 2003 CON\_01\_AE Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 95)

Figures 54A and 54B. Fig. 54A. 2003 CON\_02\_AG Env (SEQ ID NO: 94). Fig. 54B. 2003 CON\_02\_AG Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 96)

Figures 55A and 55B. Fig. 55A. 2003 CON\_03\_AB Env (SEQ ID NO: 97). Fig. 55B. 2003 CON\_03\_AB Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 99)

Figures 56A and 56B. Fig. 56A. 2003 CON\_04\_CPX Env (SEQ ID NO: 98). Fig. 56B. 2003 CON\_04\_CPX Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 100)

Figures 57A and 57B. Fig. 57A. 2003 CON\_06\_CPX Env (SEQ ID NO: 101). Fig. 57B. 2003 CON\_06\_CPX Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 103)

Figures 58A and 58B. Fig. 58A. 2003 CON\_08\_BC Env (SEQ ID NO: 102). Fig. 58B. 2003 CON\_08\_BC Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 104)

Figures 59A and 59B. Fig. 59A. 2003 CON\_10\_CD Env (SEQ ID NO: 105). Fig. 59B. 2003 CON\_10\_CD Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 107)

Figures 60A and 60B. Fig. 60A. 2003 CON\_11\_CPX Env (SEQ ID NO: 106). Fig. 60B. 2003 CON\_11\_CPX Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 108)

Figures 61A and 61B. Fig. 61A. 2003 CON\_12\_BF Env (SEQ ID NO: 109). Fig. 61B. 2003 CON\_12\_BF Env.seq.opt.  
(Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 111)

Figures 62A and 62B. Fig. 62A. 2003\_CON\_14\_BG Env (SEQ ID NO: 110). Fig. 62B. 2003\_CON\_14\_BG Env.seq.opt. (Seq.opt. = codon optimized encoding sequence.) (SEQ ID NO: 112)

Figures 63A and 63B. Fig. 63A. 2003\_CON\_S gag.PEP (SEQ ID NO: 113). Fig. 63B. 2003\_CON\_S gag.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 114)

Figures 64A and 64B. Fig. 64A. 2003\_M.GROUP.anc gag.PEP (SEQ ID NO: 115). Fig. 64B. 2003\_M.GROUP.anc gag.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 116)

Figures 65A-65D. Fig. 65A. 2003\_CON\_A1 gag.PEP (SEQ ID NO: 117). Fig. 65B. 2003\_CON\_A1 gag.OPT (SEQ ID NO: 118). Fig. 65C. 2003\_A1.anc gag.PEP (SEQ ID NO: 119) . Fig. 65D. 2003\_A1.anc gag.OPT (SEQ ID NO: 120). (OPT = codon optimized encoding sequence.)

Figures 66A and 66B. Fig. 66A. 2003\_CON\_A2 gag.PEP (SEQ ID NO: 121). Fig. 66B. 2003\_CON\_A2 gag.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 122)

Figures 67A-67D. Fig. 67A. 2003\_CON\_B gag.PEP (SEQ ID NO: 123). Fig. 67B. 2003\_CON\_B gag.OPT (SEQ ID NO: 124). Fig. 67C. 2003\_B.anc gag.PEP (SEQ ID NO: 125). Fig. 67D. 2003\_B.anc gag.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 126)

Figures 68A-68D. Fig. 68A. 2003\_CON\_C gag.PEP (SEQ ID NO: 127). Fig. 68B. 2003\_CON\_C gag.OPT (SEQ ID NO: 128).

Fig. 68C. 2003\_C.anc.gag.PEP (SEQ ID NO: 129). Fig. 68D.  
2003\_C.anc.gag.OPT. (OPT = codon optimized encoding sequence.)  
(SEQ ID NO: 130)

Figures 69A and 69B. Fig. 69A. 2003\_CON\_D gag.PEP (SEQ ID  
NO: 131). Fig. 69B. 2003\_CON\_D gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 132)

Figures 70A and 70B. Fig. 70A. 2003\_CON\_F gag.PEP (SEQ ID  
NO: 133). Fig. 70B. 2003\_CON\_F gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 134)

Figures 71A and 71B. Fig. 71A. 2003\_CON\_G gag.PEP (SEQ ID  
NO: 135). Fig. 71B. 2003\_CON\_G gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 136)

Figures 72A and 72B. Fig. 72A. 2003\_CON\_H gag.PEP (SEQ ID  
NO: 137). Fig. 72B. 2003\_CON\_H gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 138)

Figures 73A and 73B. Fig. 73A. 2003\_CON\_K gag.PEP (SEQ ID  
NO: 139). Fig. 73B. 2003\_CON\_K gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 140)

Figures 74A and 74B. Fig. 74A. 2003\_CON\_01\_AE gag.PEP  
(SEQ ID NO: 141). Fig. 7B. 2003\_CON\_01\_AE gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 142)

Figures 75A and 75B. Fig. 75A. 2003\_CON\_02\_AG gag.PEP  
(SEQ ID NO: 143). Fig. 75B. 2003\_CON\_02\_AG gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 144)

Figures 76A and 76B. Fig. 76A. 2003\_CON\_03\_ABG gag.PEP  
(SEQ ID NO: 145). Fig. 76B. 2003\_CON\_03\_ABG gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 146)

Figures 77A and 77B. Fig. 77A. 2003\_CON\_04\_CFX gag.PEP  
(SEQ ID NO: 147). Fig. 77B. 2003\_CON\_04\_CFX gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 148)

Figures 78A and 78B. Fig. 78A. 2003\_CON\_06\_CPX gag.PEP  
(SEQ ID NO: 150). Fig. 78B. 2003\_CON\_06\_CPX gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 151)

Figures 79A and 79B. Fig. 79A. 2003\_CON\_07\_BC gag.PEP  
(SEQ ID NO: 152). Fig. 79B. 2003\_CON\_07\_BC gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 153)

Figures 80A and 80B. Fig. 80A. 2003\_CON\_08\_BC gag.PEP(SEQ  
ID NO: 154). Fig. 80B. 2003\_CON\_08\_BC gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 155)

Figures 81A and 81B. Fig. 81A. 2003\_CON\_10\_CD gag.PEP(SEQ  
ID NO: 156). Fig. 81B. 2003\_CON\_10\_CD gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 157)

Figures 82A and 82B. Fig. 82A. 2003\_CON\_11\_CPX gag.PEP  
(SEQ ID NO: 158). Fig. 82B. 2003\_CON\_11\_CPX gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 159)

Figures 83A and 83B. Fig. 83A. 2003\_CON\_12\_BF.gag.PEP (SEQ  
ID NO: 160) . Fig. 83B. 2003\_CON\_12\_BF.gag.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 161)

Figures 84A and 84B. Fig. 84A. 2003\_CON\_14\_BG gag.PEP  
(SEQ ID NO: 162). Fig. 84B. 2003\_CON\_14\_BG gag.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 163)

Figures 85A and 85B. Fig. 85A. 2003\_CONS nef.PEP (SEQ ID  
NO: 164). Fig. 85B. 2003\_CONS nef.OPT. (OPT = codon optimized  
encoding sequence.) (SEQ ID NO: 165)

Figures 86A and 86B. Fig. 86A. 2003\_M GROUP.anc nef.PEP  
(SEQ ID NO: 166). Fig. 86B. 2003\_M GROUP.anc.nef.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 167)

Figures 87A and 87B. Fig. 87A. 2003\_CON\_A nef.PEP (SEQ ID  
NO: 168). Fig. 87B. 2003\_CON\_A nef.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 169)

Figures 88A-88D. Fig. 88A. 2003\_CON\_A1 nef.PEP (SEQ ID  
NO: 170). Fig. 88B. 2003\_CON\_A1 nef.OPT (SEQ ID NO: 171).  
Fig. 88C. 2003\_A1.anc nef.PEP (SEQ ID NO: 172). Fig. 88D.  
2003\_A1.anc nef.OPT. (OPT = codon optimized encoding sequence.)  
(SEQ ID NO: 173)



Figures 89A and 89B. Fig. 89A. 2003\_CON\_A2 nef.PEP (SEQ ID NO: 174). Fig. 89B. 2003\_CON\_A2 nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 175)

Figures 90A-90D. Fig. 90A. 2003\_CON\_B nef.PEP (SEQ ID NO: 176). Fig. 90B. 2003\_CON-B nef.OPT (SEQ ID NO: 177). Fig. 90C. 2003\_B.anc nef.PEP (SEQ ID NO: 178). Fig. 90D. 2003\_B.anc nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 179)

Figures 91A and 91B. Fig. 91A. 2003\_CON\_02\_AG nef.PEP (SEQ ID NO: 180). Fig. 91B. 2003\_CON\_02\_AG nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 181)

Figures 92A-92D. Fig. 92A. 2003\_CON\_C nef.PEP (SEQ ID NO: 182). Fig. 92B. 2003\_CON\_C nef.OPT (SEQ ID NO: 183). Fig. 92C. 2003\_C.anc nef.PEP (SEQ ID NO: 184). Fig. 92D. 2003\_C.anc nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 185)

Figures 93A and 93B. Fig. 93A. 2003\_CON\_D nef.PEP (SEQ ID NO: 186). Fig. 93B. 2003\_CON\_D nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 187)

Figures 94A and 94B. Fig. 94A. 2003\_CON\_F1 nef.PEP (SEQ ID NO: 188). Fig. 94B. 2003\_CON\_F1 nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 189)

Figures 95A and 95B. Fig. 95A. 2003\_CON\_F2 nef.PEP (SEQ ID NO: 190). Fig. 95B. 2003\_CON\_F2 nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 191)

Figures 96A and 96B. Fig. 96A. 2003\_CON\_G nef.PEP (SEQ ID NO: 192). Fig. 96B. 2003\_CON\_G nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 193)

Figures 97A and 97B. Fig. 97A. 2003\_CON\_H nef.PEP (SEQ ID NO: 194). Fig. 97B. 2003\_CON\_H nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 195)

Figures 98A and 98B. Fig. 98A. 2003\_CON\_01\_AE nef.PEP (SEQ ID NO: 196). Fig. 98B. 2003\_CON\_01\_AE nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 197)

Figures 99A and 99B. Fig. 99A. 2003\_CON\_03\_AE nef.PEP (SEQ ID NO: 198). Fig. 99B. 2003\_CON\_03\_AE nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 199)

Figures 100A and 100B. Fig. 100A. 2003\_CON\_04\_CFX nef.PEP (SEQ ID NO: 200). Fig. 100B. 2003\_CON\_04\_CFX nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 201)

Figures 101A and 101B. Fig. 101A. 2003\_CON\_06\_CFX nef.PEP (SEQ ID NO: 202). Fig. 101B. 2003\_CON\_06\_CFX nef.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 203)

Figures 102A and 102B. Fig. 102A. 2003\_CON\_08\_BC nef.PEP  
(SEQ ID NO: 204). Fig. 102B. 2003\_CON\_08\_BC nef.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 205)

Figures 103A and 103B. Fig. 103A. 2003\_CON\_10\_CD nef.PEP  
(SEQ ID NO: 206). Fig. 103B. 2003\_CON\_10\_CD nef.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 207)

Figures 104A and 104B. Fig. 104A. 2003\_CON\_11\_CFX nef.PEP  
(SEQ ID NO: 208). Fig. 104B. 2003\_CON\_11\_CFX nef.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 209)

Figures 105A and 105B. Fig. 105A. 2003\_CON\_12\_BF nef.PEP  
(SEQ ID NO: 210). Fig. 105B. 2003\_CON\_12\_BF nef.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 211)

Figures 106A and 106B. Fig. 106A. 2003\_CON\_14\_BG nef.PEP  
(SEQ ID NO: 212). Fig. 106B. 2003\_CON\_14\_BG nef.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 213)

Figures 107A and 107B. Fig. 107A. 2003\_CON\_S pol.PEP (SEQ  
ID NO: 214). Fig. 107B. 2003\_CON\_S pol.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 215)

Figures 108A and 108B. Fig. 108A. 2003\_M GROUP anc pol.PEP  
(SEQ ID NO: 216). Fig. 108B. 2003\_M.GROUP anc pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 218)

Figures 109A-109D. Fig. 109A. 2003\_CON\_A1 pol.PEP (SEQ ID NO: 217). Fig. 109B. 2003\_CON\_A1 pol.OPT (SEQ ID NO: 219). Fig. 109C. 2003\_A1.anc pol.PEP (SEQ ID NO: 220). Fig. 109D. 2003\_A1.anc pol.OPT (SEQ ID NO: 221). (OPT = codon optimized encoding sequence.)

Figures 110A and 110B. Fig. 110A. 2003\_CON\_A2 pol.PEP (SEQ ID NO: 222). Fig. 110B. 2003\_CON\_A2 pol.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 224)

Figures 111A-111D. Fig. 111A. 2003\_CON\_B pol.PEP (SEQ ID NO: 223). Fig. 111B. 2003\_CON\_B pol.OPT (SEQ ID NO: 225). Fig. 111C. 2003\_B.anc pol.PEP (SEQ ID NO: 226). Fig. 111D. 2003\_B.anc pol.OPT (SEQ ID NO: 227). (OPT = codon optimized encoding sequence.)

Figures 112A-112D. Fig. 112A. 2003\_CON\_C pol.PEP (SEQ ID NO: 228). Fig. 112B. 2003\_CON\_C pol.OPT (SEQ ID NO: 229). Fig. 112C. 2003\_C.anc pol.PEP (SEQ ID NO: 230). Fig. 112D. 2003\_C.anc pol.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 231)

Figures 113A and 113B. Fig. 113A. 2003\_CON\_D pol.PEP (SEQ ID NO: 232). Fig. 113B. 2003\_CON\_D pol.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 224)

Figures 114A and 114B. Fig. 114A. 2003\_CON\_F1 pol.PEP (SEQ ID NO: 233). Fig. 114B. 2003\_CON\_F1 pol.OPT. (OPT = codon optimized encoding sequence.) (SEQ ID NO: 235)

Figures 115A and 115B. Fig. 115A. 2003\_CON\_F2 pol.PEP  
(SEQ ID NO: 236). Fig. 115B. 2003\_CON\_F2 pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 238)

Figures 116A and 116B. Fig. 116A. 2003\_CON\_G pol.PEP (SEQ  
ID NO: 237). Fig. 116B. 2003\_CON\_G pol.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 239)

Figures 117A and 117B. Fig. 117A. 2003\_CON\_H pol.PEP (SEQ  
ID NO: 240). Fig. 117B. 2003\_CON\_H pol.OPT. (OPT = codon  
optimized encoding sequence.) (SEQ ID NO: 242)

Figures 118A and 118B. Fig. 118A. 2003\_CON\_01\_AE pol.PEP  
(SEQ ID NO: 241). Fig. 118B. 2003\_CON\_01\_AE pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 243)

Figures 119A and 119B. Fig. 119A. 2003\_CON\_02\_AG pol.PEP  
(SEQ ID NO: 244). Fig. 119B. 2003\_CON\_02\_AG pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 246)

Figures 120A and 120B. Fig. 120A. 2003\_CON\_03\_AB pol.PEP  
(SEQ ID NO: 245). Fig. 120B. 2003\_CON\_03\_AB pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 247)

Figures 121A and 121B. Fig. 121A. 2003\_CON\_04\_CPX pol.PEP  
(SEQ ID NO: 248). Fig. 121B. 2003\_CON\_04\_CPX pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 250)

Figures 122A and 122B. Fig. 122A. 2003\_CON\_06\_CPX pol.PEP  
(SEQ ID NO: 249). Fig. 122B. 2003\_CON\_06\_CPX pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 251)

Figures 123A and 123B. Fig. 123A. 2003\_CON\_08\_BC pol.PEP  
(SEQ ID NO: 252). Fig. 123B. 2003\_CON\_08\_BC pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 254)

Figures 124A and 124B. Fig. 124A. 2003\_CON\_10\_CD pol.PEP  
(SEQ ID NO: 253). Fig. 124B. 2003\_CON\_10\_CD pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 255)

Figures 125A and 125B. Fig. 125A. 2003\_CON\_11\_CPX pol.PEP  
(SEQ ID NO: 256). Fig. 125B. 2003\_CON\_11\_CPX pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 258)

Figures 126A and 126B. Fig. 126A. 2003\_CON\_12\_BF pol.PEP  
(SEQ ID NO: 257). Fig. 126B. 2003\_CON\_12\_BF pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 259)

Figures 127A and 127B. Fig. 127A. 2003\_CON\_14\_BG pol.PEP  
(SEQ ID NO: 260). Fig. 127B. 2003\_CON\_14\_BG pol.OPT.  
(OPT = codon optimized encoding sequence.) (SEQ ID NO: 261)

At page 39, please delete Table 1 in its entirety and  
insert the following new Table 1 in lieu thereof:

Table 1. T cell epitope mapping of CON6, JRFL and 96ZM651

Env immunogen in BALB/c mice. Table discloses SEQ ID

NOS 262-287, respectively, in order of appearance.

Peptide	Immunogen			T cell response
	CON6	JRFL (B)	96ZM651 (C)	
CON 6 (group M consensus)				
16 DTEVHNWATHACVP	+		+	CD4
48 KNSSEYYRLINCNTS	+		+	CD4
49 EYYRLINCNTSAITQ				
53 CPKVSFEPIPIHYCA	+			CD4
54 SFEPIPIHYCAPAGF				
62 NVSTVQCTHGKIPVV	+			CD4
104 ETITLPCRQIINM	+			CD8
105 LPCRIQIINMWQGV				
130 GIVQQSNLLRAIEA	+			CD4
131 VQQSNLLRAIEAQQHL				
134 AQQHLLQLTVWGIKQLQ	+			CD4
135 LQLTVWGIKQLGARVL				
Subtype B (MN)				
6223 AKAYDTEVHNWATQ	+			CD4
6224 DTEVHNWATQACVP				
6261 ACPKISFEPIPIHYC	+			CD4
6262 ISFEPIPIHYCAPAG				
6286 RKRIHIGPGRAFYTT		+		CD8
6287 HIGPGRAFYTTKNII				
6346 IVQQQNNLLRAIEAQ	+			CD4
6347 QNNLLRAIEAQQHML				
Subtype C (Chn19)				
4834 VPVWKEAKTTLFCASDAKSY			+	CD4
4836 GKEVHNWATHACVPTDNP	+		+	CD4
4848 SSENSSEYYRLINCNTSAIT	+		+	CD4
4854 STVQCTHGKIPVVSTQLLLN	+			CD4
4884 QQSNLLRAIEAQQHLLQLTV	+			CD4
4885 AQQHLLQLTVWGIKQLQTRV	+			CD4

At page 40, please delete Table 2 in its entirety and  
 insert the following new Table 2 in lieu thereof:

Table 2. T cell epitope mapping of CON6.gp120  
 immunogen in C57BL/6 mice. Table discloses SEQ ID NOS  
 288-304, respectively, in order of appearance.

Peptide	Peptide sequence	T cell response
CON 6		
(consensus)		
2	GIQRNCQHLWRWGT	CD8
3	NCQHLWRWGTMLGM	
16	DTEVHNVWATHACVP	CD4
53	CPKVSFEPIPIHYCA	CD4
97	FYCNTSGLFNSTWFM	CD8
99	FNSTWFMNGTYMFNG	CD8
Subtype B (MN)		
6210	GIRRNQYQHWGWGT	CD8
6211	NYQHWGWGTMLLGL	
6232	NMWKNNMVEQMHEDI	CD4
6262	ISFEPIPIHYCAPAG	CD4
6290	NIIGTIRQAHCNISR	CD4
6291	TIRQAHCNISRKWN	
Subtype C (Chn 19)		
4830	MRVTGIRKNYQHLWRWGTM	CD8
5446	RWGTMMLGMLMICSAAEN	CD8



4836	GKEVHNVWATHACVPTDPNP	CD4
4862	GDIRQAHCNISKDKWNETLQ	CD4
4888	LLGIWGCSGKLICTTTVPWN	CD8

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Please delete the paragraphs beginning at page 44, line 1, in their entirety and insert the following new paragraphs in lieu thereof:

As the next iteration of consensus immunogens, and in recognition of the fact that a practical HIV-1 immunogen can be a polyvalent mixture of either several subtype consensus genes, a mixture of subtype and consensus genes, or a mixture of centralized genes and wild type genes, a series of 11 subtype consensus, and wild type genes have been designed from subtypes A, B, C, CRF AE01, and G as well as a group M consensus gene from Year 2003 Los Alamos National Database sequences. The wild type sequences were chosen either because they were known to come from early transmitted HIV-1 strains (those strains most likely to be necessary to be protected against by a vaccine) or because they were the most recently submitted strains in the database of that subtype. These nucleotide and amino acid sequences are shown in Figures 28-38 (for all 140CF designs shown, 140CF gene can be flanked with the 5' sequence "TTCAGTCGACGGCCACC" (SEQ ID NO: 305) that contains a Kozak sequence (GCCACCATGG/A) (SEQ ID NO: 306) and *SalI* site and 3' sequence of TAAAGATCTTACAA (SEQ ID NO: 307) containing stop codon and *BglII* site). Shown in Figures 39-62 are 2003 centralized (consensus and ancestral) HIV-1 envelope proteins and the codon optimized gene sequences.

Major differences between CON6 gp140 (which does not neutralize non-clade B HIV strains) and Con-S gp140 (which does induce antibodies that neutralize non-clade B HIV strains) are in Con-S V1, V2, V4 and V5 regions. For clade B strains, peptides of the V3 region can induce neutralizing antibodies (Haynes et al, J. Immunol. 151:1646-1653 (1993)). Thus, construction of Th-V1, Th-V2, Th-V4, Th-V5 peptides can be expected to give rise to the desired broadly reactive anti-non-clade B neutralizing antibodies. Therefore, the Th-V peptides set forth in Table 4 are contemplated for use as a peptide immunogen(s) derived from Con-S gp140. The gag Th determinant (GTH, Table 4) or any homologous GTH sequence in other HIV strains, can be used to promote immunogenicity and the C4 region of HIV gp120 can be used as well (KQIINMWQVVGKAMYA) (SEQ ID NO: 308) or any homologous C4 sequence from other HIV strains (Haynes et al, J. Immunol. 151:1646-1653 (1993)). Con-S V1, V2, V4, V5 peptides with an N-terminal helper determinant can be used singly or together, when formulated in a suitable adjuvant such as Corixa's RC529 (Baldridge et al, J. Endotoxin Res. 8:453-458 (2002)), to induce broadly cross reactive neutralizing antibodies to non-clade B isolates.

At page 46, please delete Table 4 in its entirety and insert the following new Table 4 in lieu thereof:

Table 4 (SEQ ID NOS 309-318, respectively, in order of appearance)		
1)	GTH Con-S V1 132-150	YKRWIILGLNKIVRMYTNVNTNTTNNTEEKGEIKN
2)	GTH Con-S V2 157-189	YKRWIILGLNKIVRMYTEIRDKKQKVYALFYRLDVVPIDDDNNNNSSNYR
3)	GTH Con-S V3 294-315	YKRWIILGLNKIVRMYTRPNNNTRKSIRIGPGQAFYAT
4)	GTH Con-S V4 381-408	YKRWIILGLNKIVRMYNTSGLFNSTWIGNGTKNNNNNTNDTITLP
5)	GTH Con-S V5 447-466	YKRWIILGLNKIVRMYRDGGNNNTNETEIFRPGGGD
6)	GTH Con-6 V1 132-150	YKRWIILGLNKIVRMYNVRNVSSNGTETDNEEIKN
7)	GTH Con-6 V2 157-196	YKRWIILGLNKIVRMYTELDDKKQKVYALFYRLDVVPIDDKNSSEISGKNSSEYYR
8)	GTH-Con6 V3 301-322	YKRWIILGLNKIVRMYTRPNNNTRKSIHIGPGQAFYAT
9)	GTH Con-6 V4 388-418	YKRWIILGLNKIVRMYNTSGLFNSTWMFNGTYMFNGTKDNSETITLP
10)	GTH Con 6 V5 457-477	YKRWIILGLNKIVRMYRDGGNNSNKNKTETFRPGGGD

Please delete the paragraph beginning at page 57, line 10 and insert the following new paragraph in lieu thereof:

*Expression of CON6 gp120 and gp140 proteins in recombinant vaccinia viruses (VV).* To express and purify the secreted form of HIV-1 CON6 envelope proteins, CON6 gp120 and gp140CF plasmids were constructed by introducing stop codons after the gp120 cleavage site (REKR) (SEQ ID NO: 319) and before the transmembrane domain (YIKIFIMIVGGLIGLRIVFAVLSIVN) (SEQ ID NO: 320), respectively. The gp120/gp41 cleavage site and fusion domain of gp41 were deleted in the gp140CF protein. Both CON6 gp120 and gp140CF DNA constructs were cloned into the pSC65 vector (from Bernard Moss, NIH, Bethesda, MD) at SalI and KpnI restriction enzyme sites. This vector contains the lacZ gene

that is controlled by the p7.5 promoter. A back-to-back P E/L promoter was used to express CON6 env genes. BSC-1 cells were seeded at  $2 \times 10^5$  in each well in a 6-well plate, infected with wild-type vaccinia virus (WR) at a MOI of 0.1 pfu/cell, and 2 hr after infection, pSC65-derived plasmids containing CON6 env genes were transfected into the VV-infected cells and recombinant (r) VV selected as described (Moss and Earl, Current Protocols in Molecular Biology, eds, Ausubel et al (John Wiley & Sons, Inc. Indianapolis, IN) pp. 16.15.1-16.19.9 (1998)). Recombinant VV that contained the CON6 env genes were confirmed by PCR and sequencing analysis. Expression of the CON6 envelope proteins was confirmed by SDS-PAGE and Western blot assay. Recombinant CON6 gp120 and gp140CF were purified with agarose *galanthus Nivalis* lectin beads (Vector Labs, Burlingame, CA), and stored at  $-70^{\circ}\text{C}$  until use. Recombinant VV expressing JRFL (vCB-28) or 96ZM651 (vT241R) gp160 were obtained from the NIH AIDS Research and Reference Reagent Program (Bethesda, MD).

Before the Figures, insert the Sequence Listing submitted herewith.